FINAL REPORT

REVIEW DESCRIPTION

Review Type: Technical Systems Audit

Dates Review Performed: 5 - 6 November 2011

Reviewer: Mr. Michael Ray
National Health and Environmental Effects Research Laboratory (NHEERL)
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

Project Reviewed: "An epidemiologic health study of manganese exposure in East Liverpool, OH"

RARE Grant P.O.: Dr. Danelle Lobdell

SFSU Principal Investigator: Dr. Rosemarie Bowler

Review Locations: East Liverpool, OH

Date: 9 November 2011

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A. Completed Technical Systems Audit Checklist

1.0 BACKGROUND

1.1 OBJECTIVE

A technical systems audit (TSA) was performed November 5-6, 2011 on National Health and Environmental Effects Research Laboratory (NHEERL) RARE grant "An epidemiologic health study of manganese exposure in East Liverpool, OH". The NHEERL Project Officer for this project is Dr. Danelle Lobdell. The Principal Investigator is Dr. Rosemarie Bowler of San Francisco State University.

The primary objective of this TSA was to provide assistance to Drs. Lobdell and Bowler and their staff to help ensure that the study quality assurance (QA) and quality control (QC) procedures are appropriate for the anticipated end use of the data and that the study documentation is adequate to ensure the defensibility of the study results.

1.2 APPROACH

The following approach was used in conducting this TSA:

(1) Preliminary review of study documentation provided by the Principal Investigator (PI) This documentation consisted of the following:

- IRB Proposal entitled *An epidemiologic health study of manganese exposure in East Liverpool, OH,* including the neurophysiological test battery descriptions (8/4/11)

- IRB consent form and associated forms, standard operating procedures, and testing materials

(2) Preparation of a checklist based on information in the documentation listed in items above, to be used as a guide for conducting the TSA (see Appendix A). The checklist was sent to Dr. Bowler in advance of the scheduled TSA to permit her to complete major portions of the checklist on her own schedule. This approach was intended to provide Dr. Bowler ample opportunity to review the specific items that would be addressed in the TSA and to assemble the appropriate documentation.

(3) Conduct of the TSA according to the following schedule:

November 5 (Saturday) – East Liverpool, OH

(1) Introductory meeting with the San Francisco State University Principal Investigator and key staff
(2) Tour of the field site
(3) Observation of field staff administering consent forms and questionnaires

(4) Observation of field staff administering cognitive and neurological tests and processing blood, hair, and toenail samples
(5) Interviews with the Principal Investigator and key staff to review procedures and records at the field site and to complete the TSA checklist

November 6 (Sunday) – East Liverpool, OH

(1) Interviews with the Principal Investigator and key staff to review procedures and records at the field site and to complete the TSA checklist
(2) Exit meeting with the San Francisco State University Principal Investigator and key staff

1.3 REVIEW PARTICIPANTS

1.3.1 Reviewer

Mr. Michael Ray, NHEERL, U.S. Environmental Protection Agency (EPA), conducted the audit.

1.3.2 Project Personnel

The project personnel included Dr. Rosemarie Bowler, Dr. Harry Roels, Dr. Yangho Kim, and various other members of Dr. Bowler's staff.

2.0 SUMMARY

In completing the checklist and from the limited review of study records, there were areas that were identified as exemplary. Those findings are documented in Section 3.0. No recommendations for improvement or findings requiring corrective action were identified other than recordkeeping items. It is the reviewer's intent that the findings in this report increase the study personnel's awareness of QA and QC activities and good research practices and assist them in making changes to improve the quality of the research activities and study documentation, and to enhance the verifiability and defensibility of the study results.

3.0 EXEMPLARY FINDINGS

Interviews of each subject by Dr. Bowler allowed her to verify subject responses provided on questionnaires and allowed her to probe for additional information.

4.0 RECOMMENDATION for IMPROVEMENT

Some entries were missing from the study participant folders. Dr. Bowler should review all participant folders and call participants as needed to complete entries.

APPENDIX A

TECHNICAL SYSTEMS AUDIT CHECKLIST

TECHNICAL SYSTEMS AUDIT CHECKLIST

Title: **An epidemiologic health study of manganese exposure in East Liverpool, OH**

Review Date(s): **November 5-6, 2011** Location(s): East Liverpool, OH
NHEERL Project Officer: Danelle Lobdell, Ph.D.
SFSU Principal Investigator: Rosemarie Bowler, Ph.D.
Reviewers and Affiliations: Mike Ray, U.S. EPA NHEERL
Project Personnel Present: _Dr. Lobdell, Dr. Bowler, Dr. Roels, Dr. Kim, et al
Completed by: __Mike Ray_____

REVIEW QUESTIONS	RESPONSE			COMMENTS
	Y	N	NA	
A. **Planning Documents**				
1. Is there a written and approved protocol, research plan, or work plan for this study?	❄			IRB Proposal entitled *An epidemiologic health study of manganese exposure in East Liverpool, OH,* including the neurophysiological test battery descriptions (8/4/11)

2.	Is there a written and approved Quality Assurance Project Plan (QAPP) or QA Narrative Statement for this study? If not, briefly describe how/where QA & QC requirements and procedures for the study are documented.	❄			See A.1 above.
3.	Are written and approved OPs used in this study? If not, briefly describe how/where study procedures are documented.	❄			
4.	Are standard forms used in this study? If yes, list and note whether these are available to all anticipated users.	❄			Standard forms available to appropriate personnel for testing and blood/serum collection.
5.	Is the actual study design and conduct as specified in study planning documentation (e.g., OPs, protocols, work plans, QA plans)? If not: × Are changes/deviations clearly documented? × Briefly describe procedures for documenting changes/deviations.	❄			Incident form available for recording deviations. However, no deviations were observed.
B. Quality Objectives and Performance Criteria					
1.	Is the anticipated use of the data known and documented?	❄			Stated in the IRB proposal

2.	Have study quality objectives, consistent with anticipated data use, been established and documented?	❄			
3.	Have performance criteria for measurement data (e.g., detection limits, precision, bias) been established and documented?	❄			
4.	Are there established procedures for assessing whether quality objectives and measurement data criteria have been met? If yes, briefly describe.	❄			
5	Are there established procedures for corrective or response actions when measurement performance criteria or other quality objectives are not met?	❄			Examiners perform a final review of participant folders as part of participant checkout and ask participants to complete incomplete questionnaire responses.
6.	Are items 1-5 above consistent with study planning documentation (e.g., protocols, work plans, QA plans, OPs)? If not, are changes/deviations clearly documented?	❄			
C.	**Study Organization and Personnel**				
1.	Are all key study participants, roles, and responsibilities specified in study planning documentation?	❄			
2.	Are all study personnel those specified in study planning documentation?	❄			
3.	Is the fulfillment of these requirements documented for applicable personnel?	❄			

D. **Facilities, Equipment, and Supplies**				
1. List any key facilities and briefly describe the major activities performed in support of the study. Indicate whether each facility is adequate. If not, briefly describe areas where improvements may be desirable or necessary.				Hotel conference rooms and guest rooms for testing were adequate.
2. List below key equipment used in the study. For each item, indicate whether testing, inspections, and maintenance are conducted regularly. If yes, specify: × if acceptance testing, calibration, or inspection is done × frequency and range of calibration and calibration checks and the types of calibration standards used × person or organization responsible for performing calibration checks, inspections, and maintenance × if procedures are documented in an operating procedure × if a calibration or maintenance log is kept				Calibration checks of the CATSYS were performed at the start of each testing day by its operator. An instruction manual for the CATSYS was present.

a.				
b.				
c.				
d.				
e.				
3. Is acceptance inspection or testing performed on any supplies/reagents used in this study? If yes, list each and briefly describe inspection or testing procedures and associated acceptance criteria.			❄	All blood sampling supplies were provided by the CDC.
4. Are acceptance testing, inspection, maintenance, and calibration procedures performed as specified in study planning documentation (e.g., OP, protocols, work plans, QA plans)? If not, are changes/deviations clearly documented?			❄	
E. **Questionnaires**				
1. Briefly describe the review, approval, and distribution of any questionnaire forms used to collect subject data, including any revisions to the forms.				All questionnaires were IRB approved. National standardized tests were used. All appropriate personnel had copies of the questionnaires and test material.
2. Do the completed questionnaires indicate compliance with subject exclusion criteria? If not, explain.	❄			

3.	Were there written and approved procedures for personnel to follow when obtaining study data and consent forms from test subjects? If yes, list and note whether they were distributed to all personnel who collected data and consent forms. If not, describe how/where these procedures are documented.	❄			Data collection SOPs were present in the room where the questionnaires were administered.
4.	Are all items completed on participant questionnaires ? If not, explain.	❄	❄		Some items were missing.
F. Neurophysiological Measurements					
1.	Are calibration records clearly linked to the measurements?	❄			
2. Are the calibration ranges appropriate for the measurements taken?		❄			
3.	Are control samples run? If yes, describe.		❄		
4.	Are other routine QC checks performed? If yes, briefly describe.		❄		
5.	Are data transformations/calculations and units clearly documented?	❄			Calculations are performed by the CATSYS software.

6.	Are the dates of measurements documented?	❄			
7.	Are the persons who performed the measurements clearly identified?	❄			
8.	Are items 1-7 above performed as specified in study planning documentation (e.g., OP, protocols, work plans, QA plans)? If not, are changes/deviations clearly documented?	❄			
G. Quality Assessments					
1.	Have any of the following external or self-assessments been conducted or planned for the components of this study (e.g., support facilities, data management procedures)? If yes, briefly describe. × peer review × surveillance/site visit × technical systems audit × performance evaluation × data quality assessment	❄			This review is a technical systems audit. The NHEERL P.O. conducted a site visit.
2.	Are these assessments conducted or planned as specified in study planning documentation? If not, are changes/deviations clearly documented?	❄			

H. Record keeping and Data Management				
1. Is there an index list of all data, records, samples, and specimens to be maintained in this study?			❄	Data are in the process of being collected.
2. Are all study records (e.g., floppy disks, log books, notebooks, instrument outputs, samples/specimens, correspondence) clearly cross-referenced (e.g., by protocol #, date, experiment #)? If yes, briefly describe.	❄			Study records and samples identified as "East Liverpool Study".
3. Is there an individual responsible for compiling all study data?	❄			Dr. Bowler
4. Are study records maintained in a central file?	❄			
5. Are hand-written records recorded in numbered or otherwise uniquely identified notebooks or binders which are assigned to individual staff members?			❄	Standard forms used.
6. Are the initials of each person using a notebook or binder listed in the front?			❄	
7. Is dark permanent ink used and are corrections made with a strikeover and initialed? Is the reason for the change given?	❄	❄		Pencil used for cognitive tests per national testing requirement.

8.	Are there procedures for routine verification of all data collection and management techniques? If yes, briefly describe and note whether verifications are documented in study records.	❄			Examiners performed reviews at participant checkout. These reviews are recorded on a checklist. Dr. Bowler performs an overall review.
9.	Are data reduction and analysis procedures clearly documented?			❄	Data not yet scored and analyzed.
10.	Have data reduction and analysis procedures been validated? If yes, briefly describe. Is this documented?	❄			National standardized tests used.
11.	Are all data files and samples named according to a standard convention?	❄			
12.	Are all data records identified with a test/sample ID # and a protocol or study #?	❄			
13.	Are floppy discs, logbooks, and notebooks identified with the study/protocol #?	❄			
14.	Are items 1-13 above as specified in study planning documentation? If not, are changes/deviations clearly documented.	❄			
I. Blood, Hair, Toenail Samples					

1.	Are there written and approved procedures for the study personnel to follow when collecting, identifying, quantitating, storing, and transferring the samples? If yes, list below and note whether they have been distributed to all appropriate personnel participating in the study. If not, briefly describe how/where these procedures are documented.	❄			There was a CDC blood collection procedure available for the blood sampling/processing personnel. There were SOPs for collecting hair and toenails.
2.	Do the samples require any special handling and/or storage conditions? If yes, briefly describe the conditions and any documentation that these conditions were maintained.	❄			Blood samples must be refrigerated. Serum samples must be frozen. Blood collection, processing, and C of C records are maintained.